

(Int)
A4 a substrate being disposed in a separation cell, wherein the sample solution containing cells each containing polynucleotides and protein is supplied on a surface of the substrate, a plurality of independent areas are formed on the surface of the substrate and each of a single-stranded oligonucleotide probes each having a specific base sequence is immobilized to each of the areas;

means for applying a DC field onto a surface of one area of the areas;

means for capturing each of the cells one by one separately on each of the areas;

temperature measuring means for measuring a temperature of the surface of the substrate at one area of the areas;

heating or cooling means for heating or cooling the surface of the substrate at the one area of the areas; and

controling means for controling selectively the temperature of the surface of the substrate at the one area on the basis of a temperature information obtained by the temperature measuring means, by controlling the heating or cooling means,

wherein the controling means controls the heating or cooling means so as to heat the surface of the substrate at the one area of the areas to a first predetermined temperature to destroy the cell captured at the one area, to liberate the

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polynucleotides and the proteins from the cell captured at the one area, and to denature the polynucleotides liberated from the cell so as to obtain single-stranded polynucleotides, and the controlling means controls the heating or cooling means so as to cool a solution which contains no polynucleotide and has a pH value of 4 or lower and with which the sample solution on the substrate is replaced, to a second predetermined temperature to form hybrids between the single-stranded polynucleotides and the single-stranded oligonucleotide probes, so as to capturing single-stranded target polynucleotides;

wherein, after separating the single-stranded polynucleotides and the proteins, whereby the hybrids remain on the one area, by electrophoresis under the DC field applied onto the surface of the one area, based on a charge difference between the single-stranded target polynucleotides and the proteins, in the solution having a value of pH being 4 or lower, by flowing a washing solution into the separation cell, whereby the cells at the areas except for the one area remain on the areas and the hybrids remain on the one area, the washing solution is recovered to recover the proteins liberated from the cell;

wherein, after separating the single-stranded polynucleotides not forming the hybrids, whereby the hybrids

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remain on the one area, by electrophoresis under the DC field applied to the surface of the one area, by flowing the washing solution into the separation cell, the washing solution is recovered to recover the single-stranded polynucleotides not forming the hybrid;

wherein, after heating the surface of the substrate at the one area of the areas to denature the hybrids at the one area, so as to liberate the single-stranded target polynucleotides into solution, by flowing the washing solution into the separation cell, the washing solution is recovered to recover the single-stranded target polynucleotides liberated from the cell; and

wherein, by changing a position of the one area of the areas, the washing solution is recovered to recover, separately, the proteins, the single-stranded polynucleotides not forming the hybrid, and the single-stranded target polynucleotides, for each of the areas.

--31. An apparatus according to claim 30, wherein the cell is a white blood cell.

--32. An apparatus according to claim 30, wherein the single-stranded target polynucleotide is mRNA.

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--33. An apparatus for recovering a target polynucleotide in a cell comprising:

a substrate being disposed in a separation cell, wherein the sample solution containing cells is supplied on a surface of the substrate, and a plurality of independent areas are formed on the surface of the substrate;

capturing means for capturing each of the cells one by one separately on each of the areas;

means for applying a DC field onto a surface of one area of the areas;

temperature measuring means for measuring a temperature of the surface of the substrate at one area of the areas;

heating or cooling means for heating or cooling the surface of the substrate at the one area of the areas;

controlling means for controlling selectively the temperature of the surface of the substrate at the one area on the basis of a temperature information obtained by the temperature measuring means, by controlling the heating or cooling means; and

means for identifying the positions of the areas where the cells to be destroyed are present,

wherein the controlling means controls the heating or cooling means so as to heat the surface of the substrate at one of the identified positions to a first predetermined temperature to

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destroy the cell captured at the surface of the one of the identified positions, to liberate the polynucleotides and the proteins from the cell captured at the area of the one of the identified positions, and to denature the polynucleotide liberated from the cell so as to obtain a single-stranded polynucleotide, and the controlling means controls the heating or cooling means so as to cool a solution which contains no polynucleotide and has a pH value of 4 or lower and with which the sample solution on the substrate is replaced, to a second predetermined temperature to form hybrids between the single-stranded polynucleotides and the single-stranded oligonucleotide probes, so as to capturing single-stranded target polynucleotides;

wherein, after separating the single-stranded polynucleotides and the proteins, whereby the hybrids remain on the area of the one of the identified positions, by electrophoresis under the DC field applied onto the surface of the area of the one of the identified positions, based on a charge difference between the single-stranded target polynucleotides and the proteins, in the solution having a value of pH being 4 or lower, by flowing a washing solution into the separation cell, whereby the cells at the areas except for the area of the one of the identified positions remain on the areas and the hybrids remain on the area of the

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one of the identified positions the washing solution is recovered to recover the proteins liberated from the cell; wherein, after separating the single-stranded polynucleotides not forming the hybrids, whereby the hybrids remain on the area of the one of the identified positions, by electrophoresis under the DC field applied onto the surface of the area of the one of the identified positions, by flowing the washing solution into the separation cell, the washing solution is recovered to recover the single-stranded polynucleotides not forming the hybrid;

wherein, after heating the surface of the substrate at the one of the identified positions to denature the hybrids at the area of the one of the identified positions, so as to liberate the single-stranded target polynucleotides into solution, by flowing the washing solution into the separation cell, the washing solution is recovered to recover the single-stranded target polynucleotides liberated from the cell; and

wherein, by changing a position of the identified positions, the washing solution is recovered to recover, separately, the proteins, the single-stranded polynucleotides not forming the hybrid, and the single-stranded target polynucleotide, for each of the identified positions.

--34. An apparatus according to claim 33, wherein the cell is a white blood cell.

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--35. An apparatus according to claim 33, wherein the
single-stranded target polynucleotide is mRNA.--

REMARKS

Examination is requested.

Respectfully submitted,


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